

suggest you again call upon Foote, Cone and Belding, or other competent counsel. Then advertising and all the tools of mass selling can be united into a mighty program. You do not need us until then. The money which you would spend to retain us for the intervening period had better be put into a war chest for future use.

IN CONCLUSION

Now, your real problem is to gain strength and unity from within yourselves. You have a long way to go. The problem of whipping Federal medicine, in our viewpoint, is far less difficult than the chain-store situation and others of recent memory. The weapons are at hand. All that has been lacking so far is the will to fight—not on the part of your leadership, but on the part of the rank and file. All that is lacking is the stamina to adopt a common viewpoint, to accept the facts realistically.

We want you to visualize medicine on the move—a militant, united medicine. You have the power to make the move that will thrill you and the people of the State. Imagine every Rotary Club, Farm Bureau, newspaper and all of the people being told of this militant move of a united medicine to solve a great human problem.

Imagine the whole State organized into a great coöperative campaign under your leadership.

Imagine, if you will, the repercussions on each community, large and small, as this story is told—a story not duplicated elsewhere in the nation up to that time.

Imagine, the effect of this on your colleagues who will return from the War. Undoubtedly, they will praise you for *carrying on*, instead of *hanging on*.

Imagine the blueprint you will be making here in California for other States to follow.

Yes, ladies and gentlemen, responsibility is a twin and the name of its brother is opportunity. They go hand in hand. Seize then both the opportunity and the responsibility. We promise you, of course, difficulties and heartbreak, but also thrills and satisfaction such as you have never before experienced.

And we hold out to you a result which will crown your careers with new dignity and new prestige.

Thank you very much. (Applause.)

601 West Fifth Street.

Industrial employment must be deferred for job applicants with active tuberculosis. Since the employer has an obligation to the community with respect to rehabilitation, activity or tuberculosis lesions developing during employment should indicate a furlough for treatment; not termination of employment. The criteria for the recurrence of activity should include not only roentgenological evidence, but also increases in sedimentation rate or febrile reaction. Although these patients might not be passing infection to others at the time, employment would be against their own best interests and a serious potential danger to others.—Wayne L. Rutter, M. D. and J. W. Dugger, M. D., *Indus. Med.*, Jan., 1944.

CARBON TETRACHLORIDE POISONING*

REPORT OF CASES

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WORKERS in industrial medicine have long been aware of the potential dangers from carbon tetrachloride when used either as a solvent or a cleaner. Nevertheless, in the ten year period prior to our entrance into the war, the production of carbon tetrachloride almost doubled. Since that time its production and use have undoubtedly increased, probably because of its cheapness, availability and efficacy as a fat solvent. Consequently, cases of harmful exposure to the volatilized liquid have increased proportionately.

The dangers from this chemical have been found to be more serious than previously stated. Thus Elkins¹ has found symptoms of poisoning developing in employees even after exposure to a concentration of twenty-five parts per million. These employees were engaged in dry cleaning, spotting, multigraphing or coating, and complained primarily of nausea. Elkins concluded "that 100 parts per million usually recommended as the maximal allowable concentration for carbon tetrachloride is too high and that the correct value is not above 50 p.p.m. and probably not below 25 p.p.m." In June, 1942, Ashe and Sailer² reported a case of fatal uremia following a single exposure to carbon tetrachloride fumes. Their patient had been exposed for four hours while cleaning machinery in an elevator shaft. In October, 1942, Perry³ reported 88 cases occurring among soldiers who were engaged in cleaning their newly issued service rifles with carbon tetrachloride and who were working in the downstairs back-room of a closed two-story army barracks. Of the eighty-eight cases, two terminated fatally. In April, 1943, Captain M. D. Willcutts (MC), U.S.N.,⁴ reported three cases occurring among twenty members of an engine room crew who were working in the same room in which another group of men were cleaning the generators with a carbon tetrachloride spray. The men operating the spray guns wore masks and worked in two hour shifts. Of the three cases among the engine crew, two terminated fatally. McNally⁵ has collected reports of more than sixty cases of carbon tetrachloride poisoning, twelve of which ended fatally.

The purpose of this report is three fold: First, to add three more cases of poisoning resulting in

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The opinions or assertions contained herein are the private ones of the writers and are not to be construed as official or reflecting the views of the Navy Department or the Naval Service at Large.

one death; second, to review the various factors which apparently increase the susceptibility to poisoning, and third, to report the clinical pathology and necropsy findings.

POSSIBLE SYNERGISTIC FACTORS

It becomes apparent from a study of the cases reported in the literature and from our own cases, that various factors may play a synergistic rôle in causing poisoning by carbon tetrachloride. These include (in probable order of

importance): Consumption of alcohol, excessive exertion, eating a heavy meal and/or exposure to heat either just prior to, during, or immediately following inhaling of the vapors. Alcohol is of special importance as found by others^{7,8} including Willcutts⁴ who found that of 20 men exposed for three to four hours, only those three who had consumed considerable quantities of liquor prior to exposure, became poisoned. Similarly, in our cases, the three men who were hospitalized had consumed considerable liquor over

TABLE 1.—Laboratory Findings
Case 2. C.T.M. Admitted 7-13-43. Discharged 9-11-43.

Date	Urine Albumin	Urine Sediment	Red Blood Count	White Blood Count	Differential	Icterus Index	Blood Urea Nitrogen	Blood Nonprotein Nitrogen	Other Findings
7-14	2 +	Granular casts 5 r.b.c. PHPF*	4,330,000	8,150	Pmn. 79 Lym. 21				Kahn negative
7-20									Spinal fluid negative G.I. series negative Chest x-ray normal
7-22	3 +	Gran. and waxy casts 25-30 r.b.c. PHPF	4,370,000	7,770	Pmn. 72 Lym. 18	17.	127 mg. per 100 c.c.	208 mg. per 100 c.c.	Cholesterol, 182 mg./100 c.c. Sodium chloride, 445 mg./100 c.c.
7-27	Trace	Hyaline casts 6-8 w.b.c. PHPF					126	180	
8-4	Trace	Countless r.b.c. 10-15 w.b.c. PHPF							Urine sugar 1 + ; concentration and dilution test : fixation of specific gravity - 1010 - 1015
8-9	Negative	No casts No red blood cells					23	46	
8-17	Negative	Occasional cast No r.b.c.	3,390,000	7,450	Pmn. 58 Lym. 42	7.3	12	32	X-ray of chest—no change E.C.G. normal
9-1	Negative	Negative							

* Per high power field.

TABLE 2.—Laboratory Findings
Case 3. P.B.H. Admitted 7-12-43. Died 7-23-43.

Date	Urine Albumin	Urine Sediment	Red Blood Count	White Blood Count	Differential	Icterus Index	Blood Urea Nitrogen	Blood Nonprotein Nitrogen	Other Findings
7-12	Negative	Negative	5,130,000	4,800	Pmn. 63 Lym. 37				Kahn negative
7-13			4,950,000	9,400	Pmn. 84 Lym. 16				Sedimentation rate 4
7-14				11,600					Malaria negative
7-15						25			
7-16				7,200	Pmn. 88 Lym. 12				Sedimentation rate 1
7-19						19			
7-21							142 mg. per 100 c.c.		Cholesterol 147 mg. per 100 c.c. van den Bergh biphasic direct reaction
7-22	2 +	Occasional r.b.c.						135 mg. per 100 c.c.	CO ₂ combining power 45 volume per cent
7-23	3 +	Few Casts							

a weekend before being exposed. Possibly this augmentation of the toxic effects of carbon tetrachloride by alcohol is the result of a combined deleterious effect of both drugs upon the liver. Easton,⁶ in a recent review, states that carbon tetrachloride has two toxic effects—an immediate narcosis (similar to that following chloroform anesthesia) which follows exposure to heavy concentrations of the vapor for short periods and a secondary toxic effect characterized by acute hepatitis, acute nephritis, and a gastro-enteritis. Narcosis is not necessarily followed by secondary toxicity and, conversely, the latent toxic syndrome may appear without any immediate narcotic symptoms. Similarly McNally⁵ reports that, in experimental poisoning of dogs, there is found a narcotic effect, a toxic necrosis of the liver, renal injury, hypoglycemia, depletion of blood calcium and an enteritis. Fats and alcohol increased the toxic effects of the carbon tetrachloride. In human beings, McNally has summarized the symptoms and physical findings as follows: "Nausea, vomiting, abdominal pain, diarrhea, fever and headache appear within twenty-four hours after exposure to the volatilized liquid. Liver tenderness, icterus, hematemesis, hematuria, albuminuria, gradual rise in blood pressure, anuria and cardiac decompensation appear in a few days to several weeks. Transient hiccupping, subconjunctival hemorrhages, nose bleeds and paroxysmal coughing are reported in a few cases."

From the experimental and clinical material it is apparent that carbon tetrachloride is especially toxic to the liver so that the simultaneous use of alcohol, which is also toxic to the liver, will lead to more serious liver damage. Furthermore, from a perusal of the clinical findings listed above, it is obvious that those having nephritis, diabetes mellitus, myocardial degeneration, high blood pressure, and those known to be heavy drinkers should not be permitted to work with carbon tetrachloride.

SUMMARY OF CASE REPORTS

Three men drank heavily over a weekend and reported for duty Monday morning with "hangovers." They worked from 8:30 A.M. to 11:30 A.M. in a poorly ventilated compartment measuring ten by eleven by fifty feet in size. Three other men, who had not been drinking liquor recently, were also working in the same compartment. The men were cleaning machinery with rags soaked in carbon tetrachloride. They had volatilized approximately one and one-half quarts of the liquid in three hours when they noticed that the smell of the vapor became quite heavy. Only one of the men developed symptoms during the period of exposure. The fatal case (case 3) first felt sick at 10:00 A.M. (one and one-half hours after beginning of exposure) but continued to work until 11:30 A.M. The second victim (case 2) felt well until 6:30 P.M. that evening. The third man (case 1) had left the compartment frequently and had been exposed much

less than the first two. He showed no symptoms of poisoning until the following morning. The three non-alcoholic workers developed no symptoms and continued at their duty. The three cases may well be classified into three groups according to severity of the clinical symptoms:

REPORT OF CASES

CASE 1.—*Moderate Toxicity:*

This patient had left the compartment frequently and had been exposed much less than the first two. However, he had similar complaints on admission as the other two cases; namely nausea, vomiting, malaise, and epigastric pain. This man improved rapidly and returned to duty in two days. His clinical course was so indefinite that because of a concurrent head cold he was diagnosed as a case of catarrhal fever. The correct diagnosis, however, became apparent when the other two cases were studied and questioned.

CASE 2.—*Marked Toxicity with Recovery:*

This patient, a white man 35 years of age, was admitted with symptoms of nausea and vomiting, headache and pain in the upper abdomen. The onset was about 6:30 P.M. on the day of exposure to the carbon tetrachloride. However, the patient was at first not questioned regarding such exposure and since he himself did not realize the danger, he did not volunteer any information. Because of a history suggestive of ulcer, he was diagnosed on admission as possible duodenal ulcer. He stated that he was a steady drinker and that during the past six months he drank from one half to one pint of whiskey whenever he went ashore. This fact in his history was confirmed by contacting his executive officer, and a further admission diagnosis of cirrhosis of the liver was made. The physical findings, on admission, were surprisingly negative. His temperature was 99 degrees, pulse 84, respiration 20 and blood pressure 130 systolic and 70 diastolic. However, his first urine showed two plus albumin, granular casts and a few red blood cells in the sediment. Table I shows how definitely the picture became one of acute nephritis with azotemia. At one time, the urea nitrogen rose to 180 mg. per 100 c.c. of blood and the urine dilution-concentration test showed a fixation of the specific gravity between 1.010 and 1.015. The icterus index rose to 17 but never higher, and the patient did not exhibit visible jaundice. Therapy, in this case, consisted mainly of intravenous injections of large amounts of glucose in saline. About one month after admission, the patient had no complaints, was working around the wards and while the urine showed an occasional cast, his urea nitrogen was 12 mg. per 100 c.c. of blood and his non-protein nitrogen was 32 mg. per 100 c.c. of blood. He was discharged about two months after admission as completely cured with a final diagnosis of carbon tetrachloride poisoning.

CASE 3.—*Marked Toxicity with Fatal Termination:*

This patient, a white man 28 years of age, was exposed to carbon tetrachloride vapors at 8:30 A.M. on July 11, 1943. He began to feel ill at 10 A.M. when he complained of vague malaise and dull epigastric pain. He had a bloated feeling, became nauseated and, after eating his noon meal, began to vomit. Shortly thereafter, he developed diarrhea with watery stools about every hour. On July 12, 1943, he was admitted to the hospital. Because he had a suggestive clinical picture, an electrocardiograph was made. This showed inverted T waves in leads II and IV. At this time his temperature was 99, pulse 100, respirations 20 and blood pressure 138/72. A provisional diagnosis of "coronary occlusion" was

made, but in the next two days, the sedimentation rate was found to be normal. No leukocytosis was found and the electrocardiograph became normal, so that the diagnosis of coronary occlusion was considered unlikely. On July 14, 1943, he developed persistent nausea and vomiting. The vomitus was usually bile stained and, at times, streaked with blood. On July 16, 1943, subconjunctival hemorrhages appeared. X-ray examination, at this time, showed an enlargement of the heart shadow and some evidence of congestion in both lung fields, particularly the right base. On July 21, he showed edema of the lower extremities, a partial anuria, marked restlessness and a rapid pulse. The blood pressure rose to 170/96. Symptoms of uremia rapidly appeared and the laboratory findings (Table II) showed marked retention of non-protein nitrogenous substances and acidosis.

In this case, as in the preceding case, there was an elevation of the icterus index, which, in the presence of a normal fragility test, a biphasic direct van den Bergh and a fairly normal red blood cell count was interpreted as resulting from a hepatitis. On July 23, 1943, the patient expired rather suddenly, eleven days after admission.

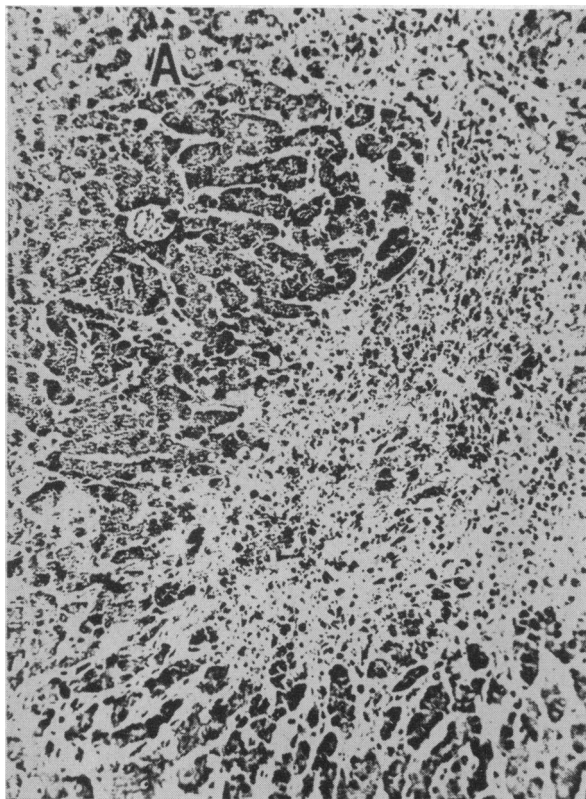


Fig. 1.—Case 3. Toxic necrosis of liver. Note central vein in upper right (A) with mid-zonal and peripheral necrosis below.

Necropsy Findings:

A summary of the necropsy findings showed the following: There was a moderate pulmonary edema. The left lung weighed 620 grams; the right lung weighed 950 grams. Both lungs showed pitting on pressure and considerable fluid oozed from the cut surfaces. The heart weighed 465 grams and was dilated so that the right border was 9.5 cm. from the midline and the left border was 11 cm. from the midline. The coronaries

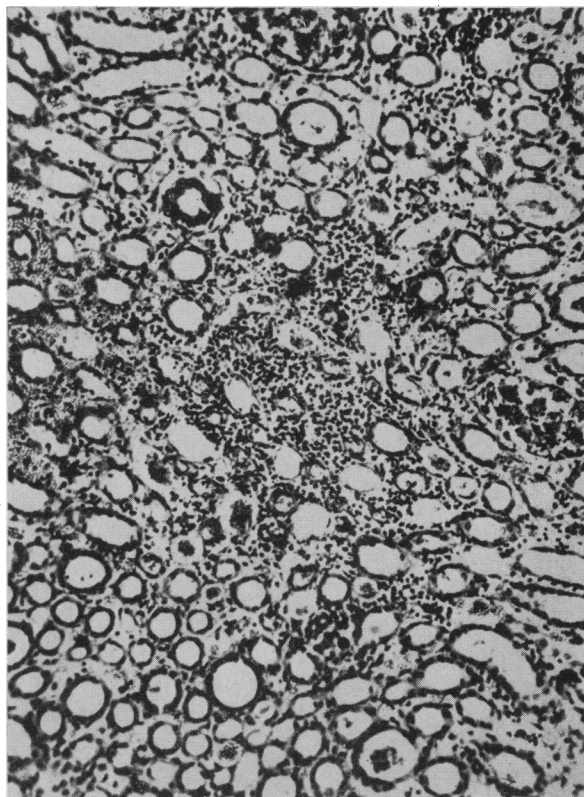


Fig. 2.—Case 3. Kidney—low power, showing interstitial collections of inflammatory cells including monocytes and frequent eosinophiles (most prominent in central section of photomicrograph).

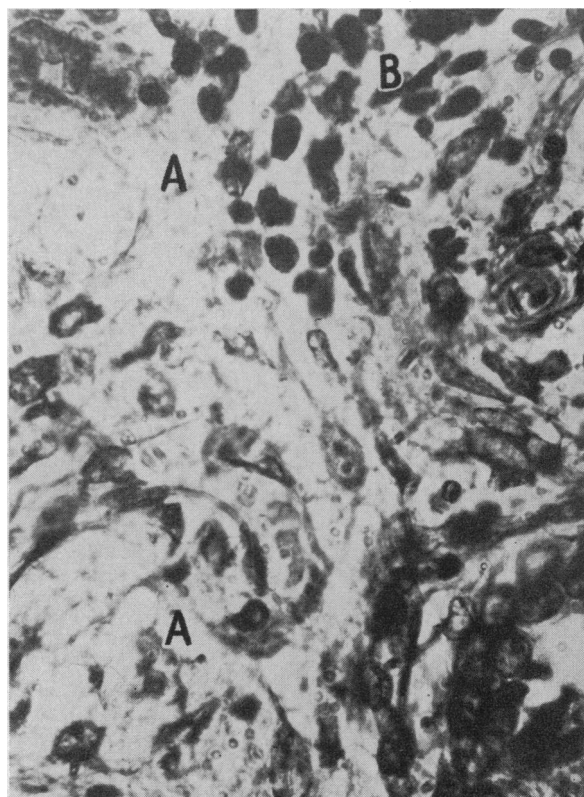


Fig. 3.—Case 3. Kidney—high power, showing interstitial edema above (at A) and inflammatory cells in interstitial tissue to right (at B).

showed no significant atherosclerosis and there was no occlusion. The liver was enlarged and weighed 1900 grams. The cut surface showed a yellow mottling. The spleen was enlarged, weighing 240 grams. Both kidneys were enlarged, each weighing 350 grams. The appearance was that of a large white kidney, and fluid oozed freely from the cut surfaces. The remaining viscera showed no significant changes from normal. The anatomic diagnoses were:

1. Acute Nephritis.
2. Pulmonary edema.
3. Cardiac dilatation.
4. Cardiac hypertrophy.
5. Hepatomegaly with toxic necrosis.
6. Splenomegaly.

COMMENT

Microscopic studies of the liver and kidney were especially interesting. Sections of the liver (Fig. 1) showed extensive focal necrosis, mainly peripheral, sometimes central. The hepatic cells in the center of such areas showed actual necrosis while the adjacent cells showed fatty and granular degenerative changes. The sinusoids were also involved with resultant leakage of red blood cells into such areas. Pigment-filled reticulo-endothelial cells were prominent. Sections of kidney (Fig. 2) showed many interstitial collections of mononuclear cells and eosinophiles. Occasional tubules contained casts. There was also present an interstitial edema and, in areas, there was interstitial hemorrhage (Fig. 3). The convoluted tubules showed considerable granular degeneration but the glomeruli did not show findings of acute glomerulitis. The microscopic findings in the kidney corresponded to what is seen in acute interstitial nephritis as described by Karsner⁹ and as seen in so-called hepatorenal syndrome and called toxic nephrosis by Smetana¹⁰ and by Corcoran et al.¹¹ The latter workers made a study of the functional changes in toxic nephrosis due to carbon tetrachloride and showed that complete recovery with normal renal function may occur. The findings in the kidney indicate that carbon tetrachloride should be considered a renal poison equivalent, in importance, to mercury.

Since we do not know definitely whether there will be any sequelae to an acute poisoning, patients once exposed and developing symptoms should not be permitted to work where they may again be exposed to carbon tetrachloride vapors. Prevention may be accomplished by education of the men as to the dangers involved, by proper ventilation, by use of masks, by rotation of jobs and, finally, by careful examination of the men. The possibility of chronic poisoning from small repeated exposures should be kept in mind.

SUMMARY

The dangers of exposure to carbon tetrachloride are presented. Carbon tetrachloride is a potent renal poison, resulting, in severe cases, in acute toxic nephrosis with uremia. Hepatitis is also found but is not marked. Alcohol ingestion prior to exposure plays a synergistic rôle.

Three cases, illustrating three grades of severity of intoxication from carbon tetrachloride, are presented. The necropsy findings of the fatal case are described and discussed.

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MEDICAL EPONYM

Weil-Felix Reaction

A paper entitled "Zur serologischen Diagnose des Fleckfiebers [Serologic Diagnosis of Typhus Fever]," by E. Weil (1880-1922) and A. Felix (b. 1887), appeared in *Wiener klinische Wochenschrift* (29:33-35, 1916). A portion of the translation follows:

"During the latter part of September, 1915, we had an opportunity to study bacteriologically, serologically and, in part, clinically, a group of cases of typhus fever in the town of R., in East Galicia. . . . Because of the coincident prevalence of typhoid fever, we were in doubt concerning the diagnosis in the first of our cases. . . . Nevertheless we were struck by the fact that no typhoid bacilli could be recovered from any of the first nine cases observed. . . . On the other hand, we cultivated a micro-organism from the urine of patient V. . . . that was not agglutinated by typhoid, paratyphoid, A and B, or dysentery antisera, but which did show agglutination with the patient's own serum in a 1:200 dilution. . . . Thirty-three cases observed in R. had been diagnosed as typhus fever. . . . All thirty-three serums gave an agglutination reaction with the bacillus under cultivation. . . . The specific agglutinins appeared at an early stage of the illness. They had reached their maximum at the time of appearance of the exanthem, persisted at this level during the febrile period of approximately fourteen days and quickly disappeared after defervescence. . . .

"We do not feel justified in regarding this germ as the provocative agent of typhus fever. . . . Nevertheless we apparently have in this microorganism a means of assistance in the diagnosis of typhus fever."

The organism is further described as a "short, delicate Gram-negative rod, resembling proteus, and weakly motile."—R. W. B., in *New England Journal of Medicine*.